ACCEPTABILITY OF HIV PRE-EXPOSURE PROPHYLAXIS (PREP) AMONG PEOPLE WHO INJECT DRUGS (PWID) IN A CANADIAN SETTING

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Abstract

A recent clinical trial provided evidence that pre-exposure prophylaxis (PrEP) has the potential to prevent HIV infection among people who inject drugs (PWID). We examined willingness to use PrEP among HIV-negative PWID in Vancouver, Canada (n=543) to inform PrEP implementation efforts. One third (35.4%) expressed willingness to use PrEP, with adjusted models indicating that younger age, no regular employment, requiring help injecting, engaging in sex work, and reporting multiple recent sexual partners were positively associated with willingness to use PrEP. Although willingness to use PrEP was low, PrEP was acceptable to some PWID at heightened risk for HIV infection.

Keywords

PrEP; PWID; Acceptability; HIV; Risk Behavior

INTRODUCTION

HIV pre-exposure prophylaxis (PrEP) has demonstrated efficacy in preventing HIV infection in several randomized trials [1–3]. Most recently, the Bangkok Tenofovir Study, a trial consisting of 2,413 people who inject drugs (PWID) in Bangkok, Thailand, has shown that a regimen of once daily oral tenofovir reduced the risk of HIV acquisition by 49% [4]. There was evidence that, as with other successful trials in non-drug users, PrEP was most efficacious among PWID with high adherence to therapy. However, important public health

questions remain, including issues regarding the effectiveness, implementation, and overall feasibility of the rollout of PrEP to PWID in real-world settings.

Initial evidence suggests that PrEP may be a cost-effective intervention among PWID [5], and although the challenges and barriers to its implementation have been a topic of active debate [6–9], few studies have examined the acceptability of and willingness to use PrEP among drug users at risk for HIV [10]. In fact, only two studies to date have published data demonstrating willingness to use PrEP among a samples of PWID, one among PWID in Ukraine [11], and more recently in Massachusetts, United States (U.S.) [12]. In the study examining Ukrainian PWID, data were collected from a sample of 128 active injectors, 86% of whom were "definitely" or "probably" willing to take PrEP [11]. Overall willingness was lower in the Massachusetts study, with only 47% of the 351 PWID noting that they would be willing to take PrEP. Further data on the acceptability of PrEP among PWID are critical to estimate the proportion that are willing to participate in PrEP regimens, and may also inform public health efforts to identify the sociodemographic characteristics and behaviors associated with higher acceptance of PrEP, and even provide early indicators of the barriers to high adherence.

The Downtown Eastside (DTES) neighborhood of Vancouver, British Columbia is home to approximately 5,000 PWID and is the center of a mature HIV epidemic [13]. Many PWID in the DTES neighborhood have access to a wide array of evidence-based HIV prevention programs, including: a supervised injection facility, needle and syringe exchange programs, opioid substitution therapy (OST), and a large-scale treatment as prevention program [14, 15]. Although the incidence of HIV among PWID in Vancouver has declined significantly over the past decade [16, 17], many HIV negative drug users remain at elevated risk for infection and thus may be eligible for PrEP under future Health Canada guidelines (in May 2014 the U.S. CDC released guidelines recommending the use of PrEP among PWID at substantial risk for HIV acquisition) [18]. Given the paucity of data available to inform PrEP implementation efforts for PWID, and since drugs use patterns and HIV risk behaviors of PWID vary substantially across different settings [19–23], the objective of this study was to describe the willingness of PWID to use PrEP in a highly resourced North American setting.

METHODS

Participants were injection drug users enrolled in the Vancouver Injection Drug Users Study (VIDUS), an open, prospective, community-recruited cohort of HIV negative PWID that began in 1996. Persons were eligible to participate in VIDUS if they resided in the Greater Vancouver region, were actively injecting drugs at enrollment (self-reported injection drug use in the past month, verified by examination for injection stigmata), and were able to provide informed consent. Given the duration of enrollment for many VIDUS cohort members, not all participants for this specific study had recently injected drugs. Between December 2012 and May 2013, 543 HIV negative VIDUS participants completed a supplemental questionnaire eliciting information regarding knowledge of and willingness to use PrEP if it were made available in the future (HIV status was ascertained by antibody assay from blood samples drawn during the study visit). Before administration of the survey, participants were asked whether they had heard of pre-exposure prophylaxis or "PrEP" for

HIV prevention. All participants, regardless of prior PrEP knowledge, were then briefly educated by trained nurses about the role of PrEP in preventing the acquisition of HIV. The nurses informed participants that PrEP can be used to reduce the risk of HIV infection in people who are HIV negative (no specific efficacy estimates were provided); that it is primarily delivered in the form of a daily pill; that PrEP has been shown to lower the chance of becoming infected from a sexual partner; that it had been approved for use in the U.S. for men who have sex with men (MSM) and heterosexual discordant couples; and finally, that studies were ongoing to determine whether PrEP can reduce the risk of infection through borrowing or sharing syringes/injection equipment. Participants were compensated $30 for their participation. The study was approved by the University of British Columbia/ Providence Health Care Research Ethics Boards.

Participants who reported willingness to use PrEP if it were made available in the future were asked two additional questions to determine whether potential side effects or the potentially low efficacy of PrEP would alter their response. The survey instrument permitted four-point Likert scale responses that ranged from "yes, definitely" willing to use PrEP to "no, definitely not." For the study analysis, the first two response options ("yes, definitely" and "yes, probably") were considered "willing," and the final two ("no, probably not" and "no, definitely not") were considered "not willing." To determine factors associated with willingness to use PrEP, we first used the Mann-Whitney test for continuous variables and Pearson's chi-square test for categorical variables in bivariable analyses. We analyzed the association between willingness to use PrEP and the following sociodemographic characteristics: age, biological sex at birth (female vs. male), non-heterosexual identity (yes vs. no), Aboriginal ancestry (yes vs. no), relationship status (ever married/common law, regular partner vs. non-regular partner/no partner), and highest level of education achieved (high school equivalent or higher vs. less than high school education). We also examined the following self-reported behaviors and exposures (occurring within the previous six months vs. no or not within the previous six months): sexual exposure to someone known to be HIV positive, any regular employment, homelessness, incarceration, syringe borrowing, requiring help injecting, any injection drug use, number of sexual partners (>1, 1 vs. 0), sex work, paying for sex with money/goods, and current enrollment in substance abuse treatment. To identify the independent correlates of willingness to use PrEP, all variables found to be significant at $p<0.05$ in bivariable analyses were entered into a multivariable logistic regression model. Using a backwards model selection procedure, we constructed the final multivariable model with the best fit (i.e., model with the lowest AIC value). All analyses were conducted using the SAS software version 9.3, and all p-values are two-sided.

RESULTS

Among 543 eligible participants, the median age was 48 years (interquartile range [IQR]: 42 – 55), 166 (30.6%) were female, and 153 (28.2%) were of Aboriginal ancestry. Only 16 (3.0%) participants reported prior knowledge of PrEP. Approximately one-third (192, 35.4%) of participants reported that they were willing to use PrEP if it were made available in the future. The bivariable associations for willingness to use PrEP are presented in Table 1. The unadjusted results show significant associations between willingness to use PrEP and the following characteristics and behaviors (all $p<0.05$): younger age (odds ratio [OR] =

1.43 per 10 years younger; 95% confidence interval [CI]: 1.18–1.74), female sex (1.52; 1.05–2.22), no regular employment (1.80; 1.16–2.79), recent incarceration (2.32; 1.14–4.71), syringe borrowing (2.15; 1.13–4.11), requiring help injecting (2.99; 1.62–5.52), any injection drug use (1.62; 1.12–2.34), multiple sexual partners (i.e., >1 vs. 0 partners [n=364]) (2.98; 1.77–5.00), and sex work (4.81; 2.39–9.70).

The results from the final multivariable model show that the following five variables were significantly and independently associated with willingness to use PrEP (all *p*<0.05): younger age (adjusted odds ratio [AOR] = 1.30 per 10 years younger; 95% CI: 1.05–1.59), no regular employment (1.67; 1.05–2.65), requiring help injecting (2.14; 1.11–4.11), and sex work (2.29; 1.01–5.20). In addition, those reporting multiple recent sexual partners (2.00; 1.07–3.74) were found to be more willing to use PrEP compared to persons with no sexual partners in the past six months.

Of the 192 (35.4%) participants who initially expressed willingness to use PrEP, this number fell to 115 (21.2%) when participants were asked if they were willing to use PrEP if they experienced known side effects of the therapy, including nausea, abdominal pain, headache and weight loss, and rarely, kidney failure or bone toxicity, as described by trained nurses. Similarly, the number of participants willing to use PrEP fell to 136 (25.0%) when interviewing nurses clarified that a daily PrEP regimen would potentially have less than 100% efficacy.

DISCUSSION

The results of this study show that, although overall PrEP acceptability was low among this sample of PWID, some sub-populations of drug users, including those at higher risk of HIV acquisition, may be willing to initiate prophylactic therapy. We observed several characteristics that may be used to identify those more willing to use PrEP, including persons: of younger age, with no regular employment, who require help injecting, who have multiple recent sexual partners, and who engage in sex work. Given previous studies demonstrating that some of these same factors are associated with an increased risk of HIV infection and greater overall vulnerability in this setting [24–26], these results are encouraging and suggest a potential role of PrEP within a comprehensive package of HIV prevention, treatment, and care services. Specifically, if future PrEP programs are able to enroll PWID with increased vulnerability to HIV infection (including through both parenteral and sexual routes of transmission), then such programs may be successful at averting incident cases, even within a context of low acceptability in the larger PWID community. Therefore, these results provide preliminary evidence that, despite early concerns from some providers that PrEP would attract interest primarily from those at lower risk (i.e., the "worried well") [27], our data indicate the opposite is possible. Finally, these results indicate that potential side effects of long-term PrEP regimens, as well as partial efficacy in the context of the demands of adherence to a daily regimen, represent important potential barriers to the implementation of PrEP interventions for PWID.

The results presented in this study differ from those published by Eisingerich, et al, [11], and Stein, et al, [12], in which overall acceptability were higher, particularly in Ukraine. These

differences are likely due to a host of social and contextual factors, including: the stage of the HIV epidemic in the respective settings, the relative availability of other HIV prevention services (including NSPs, HIV treatment access, and the availability of OST), and perhaps other cultural differences. Specifically, our results indicate that PrEP implementation and acceptability among PWID may be more challenging in mature epidemic settings such as British Columbia, with an array of existing evidence-based HIV prevention services for PWID. These results indicate that PrEP coverage levels among PWID envisioned in a recent cost effective analysis (i.e., between 25% and 50% [5]) may be difficult to achieve in a highly resourced setting such as Vancouver. Future PrEP implementation efforts among PWID in such settings should develop strategies to increase understanding of the benefits of PrEP, including prevention of sexual transmission, for those at highest risk for HIV infection. It important to note that not all of our sample may belong to a high-risk group for which PrEP is currently recommended [18], as 41% did not report any injection drug use in the prior six months. However, this does not necessarily mean that those without recent injection behavior would not be eligible for PrEP, given the sexual risk behaviors observed, and also the strong likelihood for injection drug relapse observed in other PWID populations [28]. In fact, the risk profile in our sample may actually be closer to those participating in the Bangkok Tenofovir Study (where 55% of participants did not report any injection drug use during study follow-up [4]) than the opiate users seeking detoxification surveyed by Stein, et al (where only recent injectors were eligible to participate [12]).

This study has some notable limitations. Firstly, the data were collected prior to the release of the Bangkok Tenofovir Study [4], which was the first trial to demonstrate PrEP efficacy among PWID. It is possible that following the release of the trial results, there has been an increased awareness of PrEP among communities of PWID, influencing acceptability. Indeed, awareness of PrEP prior to the survey administration was low, with only 3.0% reporting prior knowledge of the therapy. Despite this trial providing the first evidence for PrEP efficacy among PWID, given the concerns regarding imperfect efficacy in our sample, it is unclear what impact the trial results would have had on reported willingness. Finally, the educational prompt on PrEP delivered by the trained nurses may have influenced responses. Subsequently, qualitative research should be conducted to identify reasons for non-acceptability of PrEP in this and other settings.

In summary, more research is needed to determine the acceptability of and willingness to use PrEP among PWID, both in settings where there are many available evidence-based prevention modalities, and those in which there are few. Successful administration of PrEP interventions may depend heavily on the willingness of this population to enroll and adhere to what is a demanding drug regimen. However, given promising trial results demonstrating that PrEP is partially efficacious at preventing HIV infection among PWID, these interventions, packaged within comprehensive HIV prevention and treatment programs for drug users, could be considered in settings where HIV incidence in these communities persists.

Acknowledgments

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Table I

Factors associated with willingness to use PrEP if made available in the future among HIV-negative PWID in Vancouver, Canada (n=543)

Characteristic/Behavior	Willing to use PrEP n (%)[b]	Not willing to use PrEP n (%)[b]	OR (95% CI)	p–value[a]
Total	192 (35.4)	351 (64.6)		
Age (in years), Median (IQR)[f]	46 (39–53)	50 (43–55)	1.43[c] (1.18–1.74)	<0.001
Gender				
female	70 (36.5)	96 (27.4)	1.52 (1.05–2.22)	0.028
male	122 (63.5)	255 (72.6)	REF	
Non-heterosexual identity				
yes	14 (7.3)	23 (6.6)	1.11 (0.56–2.21)	0.772
no	177 (92.2)	322 (91.7)	REF	
Aboriginal ancestry				
yes	61 (31.8)	92 (26.2)	1.31 (0.89–1.93)	0.169
no	131 (68.2)	259 (73.8)	REF	
Relationship status				
ever married/common law	38 (19.8)	72 (20.5)	0.97 (0.62–1.52)	0.619
regular partner	19 (9.9)	30 (8.6)	1.17 (0.63–2.15)	0.906
non-regular partner/no partner	135 (70.3)	249 (70.9)	REF	
High school education or greater				
yes	97 (50.5)	174 (49.6)	0.99 (0.70–1.42)	0.973
no	92 (47.9)	164 (46.7)	REF	
Sex with HIV positive person[d]				
yes	9 (4.7)	8 (2.3)	2.11 (0.80–5.56)	0.124
no	174 (90.6)	326 (92.9)	REF	
No regular employment[d,f]				
yes	158 (82.3)	253 (72.1)	1.80 (1.16–2.79)	0.008
no	34 (17.7)	98 (27.9)	REF	
Homeless[d]				
yes	31 (16.1)	44 (12.5)	1.34 (0.82–2.21)	0.244
no	161 (83.9)	307 (87.5)	REF	
Incarcerated[d]				
yes	18 (9.4)	15 (4.3)	2.32 (1.14–4.71)	0.017
no	173 (90.1)	334 (95.2)	REF	
Borrowed a used syringe[d]				
yes	21 (10.9)	19 (5.4)	2.15 (1.13–4.11)	0.018
no	170 (88.5)	331 (94.3)	REF	
Required help injecting[d,f]				
yes	28 (14.6)	19 (5.4)	2.99 (1.62–5.52)	<0.001
no	163 (84.9)	331 (94.3)	REF	

Characteristic/Behavior	Willing to use PrEP n (%)[b]	Not willing to use PrEP n (%)[b]	OR (95% CI)	p–value[a]
Any injection drug use[d]				
yes	128 (66.7)	194 (55.3)	1.62 (1.12–2.34)	0.010
no	64 (33.3)	157 (44.7)	REF	
Number of sexual partners[d,f]				
>1	44 (22.9)	32 (9.1)	2.98 (1.77–5.00)	<0.001
1	56 (29.2)	120 (34.2)	1.01 (0.68–1.51)	0.960
0	91 (47.4)	197 (56.1)	REF	
Sex work[d]				
yes	28 (14.6)	12 (3.4)	4.81 (2.39–9.70)	<0.001
no	163 (84.9)	336 (95.7)	REF	
Paid money/goods for sex[d,f]				
yes	8 (4.2)	17 (4.8)	0.86 (0.36–2.02)	0.722
no	181 (94.3)	329 (93.7)	REF	
Currently enrolled in treatment[e]				
yes	127 (66.1)	204 (58.1)	1.38 (0.96–1.99)	0.086
no	65 (33.9)	144 (41.0)	REF	

Abbreviations: HIV: human immunodeficiency virus; OR: odds ratio; CI: confidence interval; IQR: interquartile range; PWID: people who inject drugs; PrEP: pre-exposure prophylaxis

[a] Based on results of Pearson's chi-square test (for categorical variables) and Mann-Whitney test (for continuous variables)

[b] Percentages do not necessarily sum to 100% due to non-response on some questions or rounding error

[c] Based on 10 year decrease in age

[d] Behaviors/activities reported in the past six months

[e] Alcohol or drug treatment

[f] Significant association (p<.05) found in the final multivariable model